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Supplemental Material

Maternal and Cord Blood Manganese Concentrations and Early Childhood Neurodevelopment among Residents near a Mining- Impacted Superfund Site

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Table S1. Variables included in multiple imputation process^a.

	Missing Values	
	Count	Percent
Prenatal exposure variables		
Maternal blood Mn	0	0.00
Maternal blood Pb	0	0.00
Maternal blood As	2	0.89
Cord blood Mn	0	0.00
Cord blood Pb	0	0.00
Cord blood As	3	1.34
Neurodevelopment variables		
Mental development index	0	0.00
Psychomotor development index	0	0.00
Child variables		
Sex	0	0.00
Gestational age at birth (weeks)	0	0.00
Birth weight (g)	0	0.00
First born child	1	0.45
Maternal variables		
Education	0	0.00
IQ	38	16.96
Hemoglobin at delivery	4	1.79
Smoked during pregnancy	0	0.00
Age at delivery (years)	0	0.00
Annual household income	66	29.46
Marital status	0	0.00
Prenatal vitamins	0	0.00
Race/Ethnicity	2	0.89

a – Prenatal exposure variables used as continuous \log_e -transformed concentrations, with Pb and As levels centered at the mean of the \log_e distribution; neurodevelopment variables, gestational age, birth weight, maternal IQ, hemoglobin at delivery, and age at delivery used as simple continuous variables; race/ethnicity (white, Native American, other), annual household income (<\$20K, \$20-40K, \$40-70K, >\$70K) used as categorical variables; sex, first born child, smoked during pregnancy, marital status, and prenatal vitamin use used as binary variables.

Table S2. Characteristics of participants with complete data on covariates included in imputation^a and participants with incomplete data.

	Participants with Complete Data (n=122)			Participants with Incomplete Data (n=102)		
	n (%)	Mean ± SD or Median (IQR)	Range	n (%)	Mean ± SD or Median (IQR)	Range
Prenatal exposure measures, median, IQR^c						
Maternal blood Mn (µg/L)	122	22.9 (18.7 – 27.4)	8.0 – 117.4	102	25.9 (20.8 – 32.6)	9.5 – 73.2
Maternal blood Pb (µg/dL)	122	0.6 (0.4 – 1.0)	0.06 – 2.9	102	0.5 (0.4 – 0.8)	0.1 – 3.0
Maternal blood As (µg/L)	122	1.9 (1.2 – 2.8)	0.5 – 7.1	100	1.7 (1.1 – 2.7)	0.2 – 8.2
Cord blood Mn (µg/L)*	122	41.5 (32.2 – 49.3)	5.4 – 87.8	102	47.0 (36.5 – 53.4)	11.5 – 139.1
Cord blood Pb (µg/dL)	122	0.4 (0.3 – 0.7)	0.01 – 3.9	102	0.4 (0.3 – 0.6)	0.03 – 3.9
Cord blood As (µg/L)	122	2.4 (1.9 – 3.5)	0.2 – 6.3	99	2.1 (1.5 – 3.1)	0.3 – 10.6
Neurodevelopment scores (mean ± SD)						
Mental development index*	122	101.1 ± 15.2	62 – 128	102	96.1 ± 16.5	54 – 128
Psychomotor development index	122	106.7 ± 11.0	61 – 129	102	103.7 ± 13.4	57 – 133
Child characteristics						
Female sex	51 (41.8)			40 (39.2)		
First born child	44 (36.1)			42 (41.6)		
Birth weight (g), mean ± SD	122	3397.7 ± 466.6	2340.0 – 4874.0	102	3413.2 ± 491.7	2296.3 – 4424.0
Gestational age at birth (weeks), mean ± SD	122	38.9 ± 1.3	36.0 – 41.0	102	39.2 ± 1.2	34.0 – 41.0
Head circumference at birth (cm), mean ± SD	118	34.8 ± 1.9	27.9 – 40.6	97	34.4 ± 1.6	30.5 – 38.7
Maternal characteristics						
Marital status: married or living with partner	100 (82.0)			74 (72.6)		
Education: ≥12 th grade	107 (87.7)			84 (82.4)		
Smoked during pregnancy: yes	29 (23.8)			27 (26.5)		
Any smokers in household: yes	26 (26.0)			24 (31.2)		
Race/Ethnicity						
White	86 (70.5)			68 (68.0)		
Native American	28 (23.0)			24 (24.0)		
Other (including Hispanic)	8 (6.6)			8 (8.0)		
Annual household income						
<\$20K	47 (38.5)			12 (33.3)		
\$20K - \$40K	41 (33.6)			13 (36.1)		

\$40K - \$70K	30 (24.6)			7 (19.4)		
>\$70K	4 (3.3)			4 (11.1)		
Hemoglobin at delivery, mean \pm SD	122	11.9 \pm 1.3	7.2 – 14.8	98	11.5 \pm 1.5	6.6 – 15.7
Age at delivery (years), mean \pm SD	122	26.5 \pm 6.2	15.0 – 43.0	102	25.1 \pm 5.1	14.0 – 41.0
IQ, mean \pm SD	122	103.5 \pm 16.9	52.0 – 134.0	64	98.7 \pm 17.9	57.0 – 135.0

a – Covariates included in imputation listed in Supplemental Table S1

b – T-tests conducted on log_e-transformed blood metals concentrations

c – Median and interquartile range (IQR, 25th to 75th percentiles) reported for blood metals concentrations.

* Participants with complete data differed from participants with incomplete data, $p < 0.05$.

Table S3. Results from multivariable^a regression models of prenatal manganese biomarkers and manganese-sex interactions with neurodevelopment.

	Outcome: MDI			Outcome: PDI		
	N	β	95% CI	N	β	95% CI
Models with Log_e Maternal Blood Manganese^b	224			224		
Maternal manganese		-4.0	-6.8, -1.3		-2.2	-4.4, 0.08
Female sex		-16.5	-50.9, 17.9		5.8	-22.0, 33.6
Maternal manganese * female sex		3.1	-1.4, 7.5		-0.3	-3.9, 3.3
Models with Log_e Cord Blood Manganese^b	224			224		
Cord manganese		-0.6	-3.6, 2.4		-0.1	-2.6, 2.3
Female sex		-13.0	-49.1, 23.1		1.7	-27.3, 30.7
Cord manganese * female sex		2.4	-1.9, 6.8		0.2	-3.2, 3.7

a – Adjusted for maternal IQ, maternal education, maternal hemoglobin, and smoothed log_e blood Pb and As (centered) in maternal or cord blood.

b – Scaled to difference between 25th and 75th percentile of blood Mn (maternal: 10.1 µg/L; cord: 18.5 µg/L).